## REMARKS

The term "derived" in claim 1 has been deleted and replaced with "cloned". The applicant submits that one skilled in the art would readily understand the meaning of the word "cloned".

Claim 7 has been amended to delete the word "modified" and to change the description "the phage vector" to "a phage vector".

Claim 9 has been amended to delete "a" before "tetracycline".

Claim 25 has been amended as suggested by the Examiner to recite, in step (c), reverse transcribing the RNA and amplifying the cDNA sequences coding for the antigen-binding fragments. The applicant submits that, in light of amendment to step (c) of claim 25, the antecedent basis for the term "the amplified cDNA" found in step (d) is now sufficient.

Claim 29 has been amended to indicate the restriction "wherein a vector employed therein is a filamentous bacteriophage".

Claims 5 and 6 have been amended to indicate that the numbers $10^9$ and $10^8$ refer to the number of clones in the library.

The Examiner is respectfully requested to reconsider and withdraw the rejection of the pending claims under 35 U.S.C. 102(b) in light of Casterman et al.

The applicant has amended claims 25 to 29 to be directed to a camelid cDNA library. Casterman et al do not teach cDNA libraries based on camelid VHs.

Casterman fails to disclose the preparation of heavy-chain antibodies by recombinant antibody/phage display technologies as claimed in the pending claims, without previous immunization of the Camelid. The quote which the Examiner has referred to on page 24, lines 15 to 16, refers to the preparation of heavy-chain antibodies by hybridoma technology. That quote is a continuation of the first paragraph on page 24 which teaches the preparation of heavy-chain monoclonal antibodies by hybridoma technology with prior immunization. Thus, the pending claims, which are directed to phage display libraries of antigen-binding fragments, fall outside that which is disclosed by Casterman.

The Examiner is respectfully requested to reconsider and withdraw the rejection of the pending claims under 35 U.S.C. 102(b) in light of Frenken [a] and [b], in light of the claim amendments, and the arguments contained herein.

The applicant has amended claim 1 to more clearly indicate that it is directed to a naïve phage display library. Frenken does not teach a naïve library, he teaches a synthetic library. Unlike naïve libraries, synthetic libraries are composed of artificial antibody fragments which have incorporated pieces of naturally occurring antibody fragments. Thus, a synthetic library is distinct from a naïve library as claimed herein.

The applicant submits that Frenken, in both citations, discloses what is described even within those documents as an "expression library". In contrast, what is claimed herein is a display library. One skilled in the art would readily understand that an expression library would not be expected to provide fragments having useful antigen binding affinity. In order to more clearly distinguish the claimed invention from the disclosure of Frenken, the applicant has amended claim 1 to indicate that the claimed library provides fragments having an antigen binding affinity with a $K_D$ of $5.7x10^{-5}$ M or lower, which one skilled in the art would readily recognize as a useful level of antigen-binding ability and not a level to be found in an expression library.

The applicant submits that, in light of the arguments and amendments herein contained, the pending claims are not obvious in light of the cited art. Briefly, Casterman teaches only an immunized library, and it would not have been obvious from Casterman that a naïve library could produce useful antigen binding fragments. Similarly, the cited references of Frenken disclose only an expression library, and fail to provide antibody fragments with useful affinity for their targets.

With respect to the reference of Hoogenboom, the applicant respectfully submits that there are significant differences between VHs and VHHs, particularly with respect to their typical binding affinities. It is a known problem in the art that naïve, or non-biased, libraries tend to produce antibodies or

antibody fragments with only very low binding affinity. VHHs typically have an even lower binding affinity than VHs do. To take Hoogenboom's approach, which was developed for the higher affinity VHs, and apply it to the production of a library of VHHs from a non-immunized animal, would not have been predicted to be successful, due to the low binding affinity observed in such a system. Thus, it would not have been obvious to one skilled in the art to combine the references of Hoogenboom, Lauwerey, and Crebber.

In light of the foregoing, the applicant submits this application is in condition for allowance.

Prompt and favourable action is respectfully requested. Should the Examiner have any concerns about the pending claims, he is invited to telephone the undersigned, to discuss these matters further.

Respectfully submitted,

Margaret McKay
Patent Agent for Applicant
Regn No: 52,519

:sta
Tel: 613-991-6853

**CERTIFICATE OF FACSIMILE TRANSMISSION**

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office on the date shown below.

Margaret McKay — September 2, 2004